REMARKS

The Office Action and the cited and applied references have been carefully reviewed. Claim 59 is allowed. Claims 1, 4-7, 12, 13, 15-17, 21-30, 36, 38, 39, 43-46, and 51-68 presently appear in this application, with claims 24-29, 46, and 51-58, 60 and 61 being withdrawn by the examiner, and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The personal interview among Mr. Roger Browdy and Dr. Allen Yun, representing applicants, and Examiner Bristol on December 15, 2009, is gratefully acknowledged. Applicants' representatives thank the examiner for the courtesies extended at the interview and confirm that the substance of the interview set forth in the Interview Summary mailed December 17, 2009, is accurate. Applicants' proposed amendments and arguments as discussed at the interview are incorporated into the amendments to the claims in this paper and into the discussion below.

Claims 15-17, 21-23, 30, 36-39 and 43-45 have been rejected under 35 U.S.C. §112, first paragraph (Enablement 1), as failing to comply with the enablement requirement for an intended use for treating or inhibiting the development of colon cancer with the inventive MHC-class I binding, CTL-inducing peptides

presented as a "cell composition". This rejection is respectfully traversed.

At the interview, it was discussed whether or not both a composition containing the peptide and a composition containing an antigen presenting cell (APC) loaded with the peptide were to be used. Applicants' representatives pointed out that the experiments in the Examples of the specification are primarily directed to using a cell line, RMA-S-HHD-B7.1, as an APC for presenting the loaded TAA peptide, and the examiner appeared to accept this argument that the specification is enabled for the cellular composition of APC presenting the loaded TAA peptide. As for the peptide composition, attached hereto is a copy of the Bar-Haim et al., *British J.Cancer* 91:398-407 (2004), publication from the laboratory of the present inventors showing that two TAA peptides found in a MAGE-8 protein in bladder cancer can individually induce CTL when administered with cholera toxin or incomplete Freund's adjuvant as adjuvant. One of skill in the art would certainly be enabled by the specification for a composition of peptides or peptide loaded APC as presently recited in the composition claims.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 3-6, 9, 12-17, 21-23, 30, 36-39, 43-45 and 62 have been rejected under 35 U.S.C. §112, first paragraph (Enablement 2) because the examiner states that the specification is lacking in enablement for any peptide isolated from any protein expressed by any polynucleotide from any human colon carcinoma cell where the peptide has the ability to bind MHC Class I and elicit a peptide-specific CTL response and where the peptide optionally includes at least one non-natural modification.

In addition, claims 5, 6, 30-45 and 59 have been rejected under 35 U.S.C. §112, first paragraph (Enablement 3), for lack of enablement for any immunogenic peptide derived from the protein encoded by the nucleotide of SEQ ID NO:58 (human 1-8D interferon inducible protein 2) or encoded by the nucleotide of SEQ ID NO:60 (human interferon inducible protein 2 polymorphism). These two rejections (enablement 2 and 3)are respectfully traversed and are argued together below, as the Interview Summary dated December 17, 2009, indicates that the discussion for enablement 3 is the same as for enablement 2.

Claim 1 is amended without prejudice to replace the recitation of "at least one non-natural modification" with "one amino acid substitution", as supported in the specification at page 33, paragraph [0072], where it is disclosed that the

peptides can be subject to changes such as "replacement of one or more amino acid residues whether dissimilar or similar". Claim 1 is also amended to recite that the claimed peptide is encoded by one of only 26 possible polynucleotides (with the possibility that the 8-10 amino acid residue peptide may have a single amino acid substitution/replacement) listed in Table 2 on page 47 of the present specification. Accordingly, the enablement issues with respect to the recitation of "at least one non-natural modification" and to any protein overexpressed by any polynucleotide in human colon carcinoma cells are believed to be obviated by the amendments to the claims.

The present specification teaches at page 46, paragraph [00111] that the protein products of the genes/polynucleotides listed in Table 2 were screened for putative HLA-A2.1 restricted peptides using the "independent binding of individual peptide side chains" software of Parker et al. *J.Immunol.* 152:163-175 (1994), made of record as Reference AK in the IDS filed February 16, 2005. This software/computer algorithm represents the structure function correlation from which one of skill in the art is enabled to arrive at the pool of putative TAA peptides on which to screen for effective binding to HLA-A2.1. The residue positions P1-P9 that are amenable to amino acid substitutions with natural amino acid residues for TAA peptides of the HLA-A2.1

haplotype are taught in paragraphs [0062]-[0068] on pages 30-32 of the present specification. The unpublished report "The effect of SNPs in Tumor Associated Antigens on the immunogenicity of peptide based vaccines" attached to the 1.132 declaration filed September 18, 2008, provide evidence demonstrating that four of four single amino acid residue substitutions of peptide 3-7 (SEQ ID NO:27) and eight of eight single amino acid residue substitutions of peptide 3-5 (SEQ ID NO:25) still retain binding to HLA.A2.1, albeit at somewhat lower affinity for four of the variants of peptide 3-5 (see paragraph bridging pages 1-2 of the Summary). Accordingly, all twelve of the single amino acid substitution variants of peptides 3-7 and 3-5 tested retain binding to HLA-A2.1.

Based on the guidance provided by the present specification and the knowledge in the art, not only is one of skill in the art enabled for TAA peptides that bind HLA-A2.1, this same person would also be enabled for whatever TAA peptides encoded by the 26 polynucleotides recited in the present claims would best be applicable to other haplotypes besides HLA-A2.1. This person of skill in the art would model peptides from the 26 overexpressed genes/polynucleotides against a particular haplotype using an art available computer algorithm/software to find putative TAA peptides to screen by repeating the tests using

the APCs of the haplotype of interest and mice that are transgenic for that particular human haplotype. See the two HLA molecule binding prediction software programs at www-bimas.cit.nih.gov/molbio/hlabind/ and www.syfpeithi.de/ (copies of the homepage for these prediction software programs are attached hereto) that were publicly available at the time the present invention was made. In addition, attached hereto are copies of the following prior art references regarding HLA molecule binding motifs:

HLA	**Reference**
A2, B27	Parker et al., *J. Biol. Chem.*, 267(8):5451-5459 (1992)
A3	Honma et al., *J. Neuroimmunol.*, 73 :7-14 (1997)
A24, Cw3	Falk et al., *Nature*, 351:290-296 (1991)
A26 family	Yamada et al., *Tissue Antigens*, 54:325-332 (1999)
A30 family	Krausa et al., *Tissue Antigens*, 56:10-18 (2000)
B7, B8, B27, B35, B51,...	Sidney et al., *J. Immunol.*, 154 :247-259 (1995)
B14	DiBrino et al., *J. Biol. Chem.*, 269(51):32426-32434 (1994)
Cw3, Cw4, Cw6, Cw7,...	Falk et al., *PNAS*, 90:12005-12009 (1993)
G	Münz et al., *J. Reprod. Immunol.*, 43:1390155 (1999).

The above list of prior art references on HLA molecule binding motif and binding prediction is not exhaustive, as there are more references known and available to the public. Thus, one of skill in the art would expect that TAA peptides from the 26 polynucleotides overexpressed in human colon carcinoma for the

other haplotypes would be found without any undue experimentation.

Reconsideration and withdrawal of the rejections are therefore respectfully requested.

Claims 1, 3-6, 9, 12-17, 21-23, 30, 36-39, 43-45 and 62-64 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement because the claims recite the negative proviso "is not a transmembrane epithelial antigen of the prostate (STEAP) protein" in claim 1, which does not find original support in the specification. This rejection is respectfully traversed.

As discussed above, applicants have amended the claims (1) to delete the recitation of "at least one non-natural modification", (2) to recite that the TAAs, from which the TAA peptides are obtained, are encoded by only 26 polynucleotides overexpressed in human colon carcinoma, and (3) to delete the negative proviso from the claims. Furthermore, in view of the amendments to the claims, the seven TAA peptides 3-7, 1-6, 3-5, 1-11, 2-3, 3-1, and 3-2 specifically disclosed in the present specification (see paragraph [00113] and the underlined peptides in Table 3 on page 49) and recited in claims 7 and 63-68 (claims 65-68 are newly added) provide a representative number of species/examples of the genus of TAA peptides encompassed by the

present claims, with structure function correlation provided by the computer algorithms/software known in the art for specific haplotypes. Accordingly, written description under 112, first paragraph, is satisfied.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

Claims 2, 12, 13, 14, 15, 16, 21, 22 and 23 have been rejected under 35 U.S.C. §102(a) as being anticipated by Tsang et al., *Cancer Res*. 61:7568-7576 (2001). This rejection is respectfully traversed.

Claim 1 amended to recite that the TAA peptide is encoded by a polynucleotide overexpressed in human colon carcinoma cells selected from the Markush group of the 26 specific genes listed in Table 2, page 47 of the present specification. None of the recited polynucleotides encode CEA and therefore cannot be anticipated by Tsang's 9-mer CTL epitope CAP-6D. Accordingly, claim 1 and claims dependent therefrom are not anticipated by Tsang.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 3, 12, 13, 14, 15, 21, 22, 23 and 62 have been rejected under 35 U.S.C. §102(a) as being anticipated by

Trojan et al., *Lung Cancer*, 36(2):151-158 (2002). This rejection is respectfully traversed.

Trojan's disclosed immunogenic peptide ILYENNVIT (184-192) of Ep-CAM and single substitution variant thereof ILYENNVIV cannot anticipate claim 1 as amended, and claims dependent therefrom since the recited peptide is not a peptide of EP-CAM, or a single substitution peptide variant thereof.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1, 12, 13, 14, 15, 16, 21, 22 and 23 have been rejected under 35 U.S.C. §102(b) as being anticipated by Abrams et al., *Cell. Immunol.* 182:137-151 (1997). This rejection is respectfully traversed.

None of the polynucleotides recited in amended claim 1 encode K-ras protein, and therefore the presently claimed peptide cannot be anticipated by Abrams. Accordingly, claim 1 and claims dependent therefrom are not anticipated by Abrams.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Copies of the Sullenberger et al., *Nature* 418:252-258 (2002); Nair et al., *Ann. Surg.* 235:540-549 (2002); Van Tendeloo et al., *Blood* 98:49-56 (2001); and Ponsaerts et al., *Leukemia* 16:13224-13230 (2002) references cited and discussed in the 1.132

declaration filed June 17, 2009, but not previously provided, are attached.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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